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Re: 09/457,931.
For use during the Interview @ 3pm (Eastern time). Thanks

Draft

Proposed claim amendments for the purpose of discussion during the Interview dated Nov. 28, 2001

TOXICITY TYPING USING EMBRYOID BODIES

By: H. Ralph SNODGRASS

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1. (Amended) A method of creating a molecular profile of a chemical composition suspected of toxicity, comprising the steps of:

a) contacting an isolated mammalian embryoid body with the chemical composition; and

b) detecting and recording alterations in expression of sets of genes or proteins[gene expression or protein expression] in the mammalian embryoid body in response to the chemical composition compared to expression of sets of gene or proteins in an embryoid body not contacted with the chemical composition, to create a [molecular profile of] pattern of alterations in gene expression or protein expression in the mammalian embryoid body in response to the chemical composition.

2. (Amended) A method of compiling a library of molecular profiles of chemical compositions having predetermined toxicities, comprising the steps of:

a) contacting an isolated mammalian embryoid body with a chemical composition having predetermined toxicities;

b) detecting and recording alterations in expression of sets of genes or proteins[gene expression or protein expression] in the mammalian embryoid body in response to the chemical composition compared to gene expression or protein expression in an embryoid body not contacted with the chemical composition, to create a [molecular profile of]pattern of alterations in expression of sets of genes or proteins in the mammalian embryoid body in response to the chemical composition; and

c) compiling a library of molecular profiles by repeating steps a) and b) with at least two chemical compositions having predetermined toxicities.

3. The method of claim 1 or 2, wherein the alterations in gene expression or protein expression are detected by a label.

4. The method of claim 3, wherein the label is selected from the group consisting of fluorescent, colorimetric, radioactive, enzyme, enzyme substrate, nucleoside analog, magnetic, glass, latex bead, colloidal gold, and electronic transponder.

Withdrawn

5. The method of claim 1 or 2, wherein the molecular profile comprises alterations in gene expression.

6. The method of claim 5, wherein the alterations in gene expression are detected by a nucleotide hybridization assay.

7. The method of claim 1 or 2, wherein the molecular profile comprises alterations in protein expression.

8. The method of claim 7, wherein the alterations in protein expression are detected by an [immunoactivity]immunodetection assay.

9. The method of claim 7, wherein the alterations in protein expression are detected by a mass spectrometry assay.

10. The method of claim 2, wherein the isolated mammalian embryoid bodies are of human.

11. The method of claim 10, further wherein the chemical compositions having predetermined toxicities are selected from the group consisting of therapeutic agents, neurotoxins, renal toxins, hepatic toxins, toxins of hematopoietic cells, and myotoxins.

12. The method of claim 10, further wherein the chemical compositions having predetermined toxicities are selected from the group consisting of agents that are toxic to cells of one or more reproductive organs, teratogenic agents and carcinogens.

13. The method of claim 10, further wherein the chemical compositions having predetermined toxicities are selected from the group consisting of agricultural chemicals, cosmetics, and environmental contaminants.

14. The method of claim 2, wherein the isolated mammalian embryoid bodies are of non-human mammals.

15. The method of claim 14, wherein the non-human mammals are rodents.

16. The method of claim 14, further wherein the chemical compositions having predetermined toxicities are selected from the group consisting of animal therapeutics, neurotoxins, renal toxins, hepatic toxins, toxins of hematopoietic cells, and myotoxins.

17. The method of claim 14, further wherein the chemical compositions having predetermined toxicities are selected from the group consisting of agents that are toxic to cells of one or more reproductive organs, teratogenic agents and carcinogens.

18. The method of claim 14, further wherein the chemical compositions having predetermined toxicities are selected from the group consisting of agricultural chemicals, cosmetics, and environmental contaminants.

Withdrawn

19. A library of molecular profiles of chemical compositions having predetermined toxicities, produced by a method according to any one of the claims 2, 10-18.

20. The library of claim 19, wherein the library comprises molecular profiles for at least 20 chemical compositions.

21. (Amended) A method of typing toxicity of a test chemical composition, comprising the steps of:

a) creating a molecular profile of the test chemical composition [according to claim 1], comprising the steps of:

i) contacting an isolated mammalian embryoid body with the chemical composition; and

ii) detecting and recording alterations in expression of sets of genes or proteins in the mammalian embryoid body in response to the chemical composition compared to expression of sets of genes or proteins in an embryoid body not contacted with the chemical composition, to create a pattern of alterations in gene expression or protein expression ; and

b) comparing the molecular profile in step a) with the molecular profile of a chemical composition having predetermined toxicities;

wherein the type of toxicity of the test chemical composition is determined by the comparison in step b).

22. A systematic method of typing toxicity of a test chemical composition, comprising the steps of:

a) creating a molecular profile of the test chemical composition[according to claim 1], comprising the steps of:

i) contacting an isolated mammalian embryoid body with the chemical composition; and

ii) detecting and recording alterations in expression of sets of genes or proteins in the mammalian embryoid body in response to the chemical composition compared to expression of sets of genes or proteins in an embryoid body not contacted with the chemical composition, to create a pattern of alterations in gene expression or protein expression; and

b) comparing the molecular profile in step a) with a composite library of molecular profiles of chemical compositions having predetermined toxicities, wherein the composite library comprises the molecular profiles of at least two chemical compositions, wherein said molecular profiles are created according to claim [1]2;

wherein the type of toxicity of the test chemical composition is determined by the comparison in step b).

23. (Amended) A method of ranking toxicity of a test chemical composition, the method comprising:

a) creating a [molecular profile of]pattern of alterations associated with of the test chemical composition [according to claim 1], comprising the steps of:

i) contacting an isolated mammalian embryoid body with the chemical composition; and

ii) detecting and recording alterations in expression of sets of genes or proteins in the mammalian embryoid body in response to the chemical composition compared to expression of sets of genes or proteins in an embryoid body not contacted with the chemical composition, to create a pattern of alterations in gene expression or protein expression ; and

b) comparing the molecular profile in step a) with a composite library of molecular profiles of chemical compositions having predetermined toxicities, wherein the composite library comprises the molecular profiles of at least two chemical compositions, said molecular profiles are created according to claim [1]2;

wherein the toxicity of the test chemical composition is ranked by the comparison in step b).

24. The method of claim 21, 22 or 23, wherein the test chemical composition is known or unknown.

25. The method of claim 21, 22 or 23, further wherein the isolated mammalian embryoid bodies are of human.

26. The method of claim 25, further wherein the chemical compositions having predetermined toxicities are therapeutic agents, neurotoxins, renal toxins, hepatic toxins, toxins of hematopoietic cells, or myotoxins.

27. The method of claim 25, further wherein the chemical compositions having predetermined toxicities are selected from the group consisting of agents that are toxic to cells of one or more reproductive organs, teratogenic agents and carcinogens.

28. The method of claim 25, further wherein the chemical compositions having predetermined toxicities are selected from the group consisting of agricultural chemicals, cosmetics, and environmental contaminants.

29. The method of claim 21, 22 or 23, further wherein the isolated mammalian embryoid bodies are of non-human mammals.

30. The method of claim 29, wherein the non-human mammals are rodents.

31. The method of claim 29, further wherein the chemical compositions having predetermined toxicities are selected from the group consisting of animal therapeutics, neurotoxins, renal toxins, hepatic toxins, toxins of hematopoietic cells, and myotoxins.

32. The method of claim 29, further wherein the chemical compositions having predetermined toxicities are selected from the group consisting of agents that are toxic to cells of one or more reproductive organs, teratogenic agents and carcinogens.

33. The method of claim 29, further wherein the chemical compositions having predetermined toxicities are selected from the group consisting of agricultural chemicals, cosmetics, and environmental contaminants.